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NEWS	3	Jan 18	ESBIOBASE - NEW FREE DISPLAY FORMATS, TRIAL FORMAT ENHANCED
NEWS	4	Feb 1	Addition of Machine-Translated Abstracts to CAplus
NEWS	5	Feb 2	STEREO BOND SEARCH PROBLEM FIXED WITH STN EXPRESS 5.0C
NEWS	6	Feb 14	Homology Searching for Nucleotide Sequences in DGENE now available!
NEWS	7	Feb 16	BIOTECHNOBASE NOW ON STN
NEWS	8	Feb 22	New Database Producer Clusters Now Available on STN
NEWS	9	Feb 28	Structure Search Limits Increased in REGISTRY, ZREGISTRY, and CASREACT
NEWS	10	Feb 28	Patent Information Now Searchable in CAOLD
NEWS	11	Mar 1	New IMSDIRECTORY Provides Pharma Company Details

NEWS EXPRESS	FREE UPGRADE 5.0C NOW AVAILABLE
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
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FILE 'HOME' ENTERED AT 09:57:12 ON 07 MAR 2000

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'REGISTRY' ENTERED AT 09:57:40 ON 07 MAR 2000
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STRUCTURE FILE UPDATES: 6 MAR 2000 HIGHEST RN 258289-79-1
DICTIONARY FILE UPDATES: 6 MAR 2000 HIGHEST RN 258289-79-1

TSCA INFORMATION NOW [redacted]RRENT THROUGH JANUARY 13, 199[redacted]

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> s futhan/cn

L1 1 FUTHAN/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN 82956-11-4 REGISTRY
CN Benzoic acid, 4-[(aminoiminomethyl)amino]-, 6-(aminoiminomethyl)-2-naphthalenyl ester, dimethanesulfonate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6-Amidino-2-naphthyl p-guanidinobenzoate
CN FUT 175
CN **Futhan**
CN Nafamostat mesilate
CN Nafamostat mesylate
MF C19 H17 N5 O2 . 2 C H4 O3 S
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CBNB, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IMSDIRECTORY, IPA, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)

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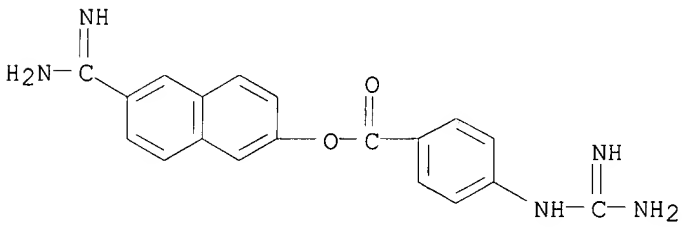
CRN 81525-10-2
CMF C19 H17 N5 O2



CM 2

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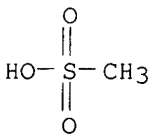

204 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
206 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> index bioscience [redacted]ents

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
FILE 'APIPAT2' ACCESS NOT AUTHORIZED
FILE 'PAPERCHEM' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     6.82       6.97

INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, AQUASCI,
       BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, CABA,
CANCERLIT,
       CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
DRUGB,
       DRUGLAUNCH, DRUGMONOG2, DRUGNL, ...' ENTERED AT 10:01:09 ON 07 MAR 2000

70 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s l1

          0*  FILE ADISALERTS
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          0*  FILE DRUGU
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          0*  FILE GENBANK
          0*  FILE HEALSAFE
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   6 FILES HAVE ONE OR MORE ANSWERS,    70 FILES SEARCHED IN STNINDEX

L2    QUE L1

=> s myocardial infarction?

       17745   FILE ADISALERTS
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         992   FILE CABA
        2499   FILE CANCERLIT
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         260   FILE HEALSAFE
         569   FILE IFIPAT
       18798   FILE JICST-EPLUS
         879   FILE LIFESCI
       91566   FILE MEDLINE
         355   FILE NIOSHTIC
         615   FILE NTIS
         198   FILE PHAR
           7   FILE PHIC
        1750   FILE PHIN
        2552   FILE PROMT
       62365   FILE SCISEARCH
       10824   FILE TOXLINE
        4304   FILE TOXLIT
        5472   FILE USPATFULL
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        3291   FILE WPINDEX
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        166    FILE PATOSWO
          1    FILE PIRA
          1    FILE RAPRA

  59 FILES HAVE ONE OR MORE ANSWERS,    70 FILES SEARCHED IN STNINDEX

L3   QUE MYOCARDIAL INFARCTION?

=> s l2 and l3

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   0 FILES HAVE ONE OR MORE ANSWERS,    70 FILES SEARCHED IN STNINDEX

L4   QUE L2 AND L3

=> file caplus, uspatfull, biosis, medline
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FULL ESTIMATED COST | 2.70 | 9.67

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FILE 'MEDLINE' ENTERED AT 10:04:28 ON 07 MAR 2000

=> d his

(FILE 'HOME' ENTERED AT 09:57:12 ON 07 MAR 2000)

FILE 'REGISTRY' ENTERED AT 09:57:40 ON 07 MAR 2000
L1 1 S FUTHAN/CN

INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, CABA, CANCERLIT, CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, ...' ENTERED AT 10:01:09 ON 07 MAR 2000

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                1   FILE RAPRA
L3             QUE MYOCARDIAL INFARCTION?
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               SEA L2 AND L3
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L4             QUE L2 AND L3
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     FILE 'CAPLUS, USPATFULL, BIOSIS, MEDLINE' ENTERED AT 10:04:28 ON 07 MAR
     2000

=> s l1

L5          338 L1
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=> s myocardial infa[redacted]ion?

L6 166534 MYOCARDIAL INFARCTION?

=> s l5 (p) l6

L7 0 L5 (P) L6

=> s l5 and l6

L8 1 L5 AND L6

=> d

L8 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:475040 BIOSIS
DN PREV199800475040
TI Interleukin-6 derived from hypoxic myocytes promotes neutrophil-mediated reperfusion injury in myocardium.
AU Sawa, Yoshiki (1); Ichikawa, Hajime; Kagisaki, Koji; Ohata, Toshihiro; Matsuda, Hikaru
CS (1) First Dep. Surg., Osaka Univ. Med. Sch., 2-2 Yamada-oka, Suita, Osaka 565 Japan
SO Journal of Thoracic and Cardiovascular Surgery, (Sept., 1998) Vol. 116, No. 3, pp. 511-517.
ISSN: 0022-5223.
DT Article
LA English

=> s disorder?

L9 1124119 DISORDER?

=> s l5 and l9

L10 37 L5 AND L9

=> s treat? or prevent?

L11 7287122 TREAT? OR PREVENT?

=> s l11 and l10

L12 28 L11 AND L10

=> d 1-28 ab,bib

L12 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB In this uncontrolled, unblinded efficacy study, 33 patients with disseminated intravascular coagulation (DIC) or the prodromal stage (preDIC) of the condition were **treated** with nafamostatmesylate (NM) administered intermittently to examine whether this regimen would be as efficacious as the std. regimen without causing an increase in drug toxicity. Efficacy was evaluated on the basis of the results of coagulation studies and on improvement in the DIC score, which was calcd. by adding the points of the underlying diseases, clin. symptoms, prothrombin ratio, fibrinogen, and fibrin degrdn. product (FDP)-E fraction. A score of 3 points was categorized as preDIC, and 4 or more as DIC. In Japan, the FDP-E fraction is often measured as a substitute for FDP because the value of the FDP-E fraction changes in a wider range and shows more sensitive responses than FDP. NM is usually given by 24-h continuous administration; in this study, NM was infused intermittently at

a daily dose of [redacted] to 150 mg i.v. to avoid hyper[redacted]emia. Each infusion lasted 4 h, and the interval between administrations was 2.95 .+-. 0.19 h.

After 7 days of **treatment**, the mean DIC score decreased significantly from 3.9 .+-. 0.1 to 2.0 .+-. 0.2 ($P < 0.001$); after 14 days of **treatment**, the score was 2.0 .+-. 0.2 ($P < 0.001$); at the end of **treatment**, the score was 1.3 .+-. 0.2 ($P < 0.001$). The improvement in clin. symptoms was considered to be excellent in 8 of 33 patients and good in 16, for an efficacy rate of 72.7% (24 of 33). Although the mean serum potassium level increased significantly, no patient developed hyperkalemia. The administration of NM in intermittent divided doses was found to be highly effective in the **treatment** of DIC in patients with the hemopoietic malignancies.

AN 1996:261622 CAPLUS
DN 124:332455
TI Effects of intermittent nafamostat mesylate in divided doses in patients with disseminated intravascular coagulation occurring with hematopoietic malignancies
AU Yonekura, Shuji; Umeda, Yoshikatsu; Ogawa, Yoshiaki; Watanabe, Shigeki; Kawada, Hiroshi; Masumoto, Akira; Fukuda, Ryuki; Sasao, Tamotsu; Nagao, Tadami
CS School Medicine, Tokai University, Isehara, Japan
SO Curr. Ther. Res. (1996), 57(3), 203-14
CODEN: CTCEA9; ISSN: 0011-393X
DT Journal
LA English

L12 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB A review with 79 refs. of pharmacol. effects of the protease inhibitor nafamostat mesilate and its efficacy in **treating** disseminated intravascular coagulation, cerebral vasospasm, and acute pancreatitis.
AN 1995:838385 CAPLUS
DN 123:274874
TI Nafamostat mesilate
AU Okajima, Kenji; Uchiba, Mitsuhiro; Murakami, Kazunori
CS Medical School, Kumamoto University, Kumamoto, Japan
SO Cardiovasc. Drug Rev. (1995), Volume Date 1995, 13(1), 51-65
CODEN: CDREEA; ISSN: 0897-5957
DT Journal; General Review
LA English

L12 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB Nafamostat mesylate (NM), a synthetic protease inhibitor, is frequently used for the **treatment** of disseminated intravascular coagulation (DIC) in Japan. NM inhibits several proteases which may be importantly involved in the pathophysiol. of DIC. Since tissue factor (TF) plays a crit. role in DIC assocd. with septicemia, inhibition of the extrinsic pathway of coagulation by coagulation inhibitors may be useful for the **treatment** of DIC. NM inhibited extrinsic pathway activity (TF-F.VIIa mediated-F.Xa generation) in a concn. dependent manner; the IC50 was 1.0 .times. 10-7 M. F.Xa was not inhibited by NM at the concns. used in the expt., suggesting that NM might inhibit TF-F.VIIa complex activity. When incubation with TF-F.VIIa complex, NM inhibited the complex activity with an IC50 of 1.5 .times. 10-7 M, the same value that found for inhibition of extrinsic pathway activity. A Lineweaver-Burk's plot of the inhibition demonstrated that NM inhibited TF-F.VIIa complex in a competitive fashion, with an inhibition const. (Ki) of 2.0 .times. 10-7 M. These findings suggested that NM may be a potent inhibitor of TF-F.VIIa complex and the therapeutic effect of NM in DIC patients could be partly explained by inhibition of the extrinsic pathway of the coagulation system.
AN 1994:260934 CAPLUS
DN 120:260934
TI Effect of nafamostat mesylate, a synthetic protease inhibitor, on tissue

factor-factor V[redacted] complex activity
AU Uchiba, Mitsuhi[redacted] Okajima, Kenji; Abe, Hiroki; [redacted]abe, Hiroaki; Takatsuki, Kiyoshi
CS Dep. Med., Kumamoto Univ. Med. Sch., Kumamoto, 860, Japan
SO Thromb. Res. (1994), 74(2), 155-61
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English

L12 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB Effect of nafamostat mesilate on the canine kidney Na, K-ATPase activity and human erythrocyte Na, K-pump activity was studied. Nafamostat mesilate dose-dependently inhibited the Na, K-ATPase activity(IC50 being 3.2 x 10-5M) and the Na, K-pump activity (IC50 10-4M). The nafamostat mesilate metabolites amidinonaphthol and p-quanidinobenzoic acid had no such effect. Hyperkalemic state in some nafamostate mesilate-**treated** patients may be due to inhibition of Na, K-ATPase.
AN 1994:95144 CAPLUS
DN 120:95144
TI Effect of a protease inhibitor, nafamostat mesilate on sodium-potassium pump activity
AU Kojima, Shunichi
CS Dep. Med., Natl. Cardiovasc. Cent. Hosp., Japan
SO Yakuri to Chiryo (1993), 21(6), 1729-34
CODEN: YACHDS; ISSN: 0386-3603
DT Journal
LA Japanese

L12 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The fragments of fibrin/fibrinogen degrdn. products (FDP) were characterized in 4 patients with disseminated intravascular coagulation (DIC), that were caused by various diseases. In the patients with acute lymphoblastic leukemia (case 1) and acute suppurative cholangitis (case 3), DD and DY/X fragments resulting from fibrinolysis accounted for the most part of the FDP fragments. In case 3, D fragments resulting from fibrinogenolysis were also obsd. to much less extent. In a DIC assocd. with acute myeloblastic leukemia (case 2), both fibrinolysis and fibrinogenolysis were increased and resulted in high levels of D, Y and DY/X fragments, concomitant with moderate levels of DD and high mol. wt. (HMW) fragments in the patient's sera. The increased fibrinogenolysis in this case was attributed to accelerated activation of plasmin. In a DIC patient of case 4, who underwent an operation due to hepatocellular carcinoma, marked increase in DY/X and HMW fragments and slight increase in DD fragment were obsd. on the day of operation. Hyperfibrinolysis documented in case 4 was explained by both increased prodn. of thrombin and moderately accelerated activation of plasmin. Both qual. and quant. change in the fragments of FDP during the courses of **treatment** in 2 cases of DIC were also noted. In summary, each underlying disease expresses characteristic pattern of FDP fragments in DIC.
AN 1993:57378 CAPLUS
DN 118:57378
TI Studies on the fragments of FDP in 4 patients with DIC
AU Okumura, Nobuo; Furuwatari, Chizumi; Ishikawa, Shinsuke; Furihata, Kenichi; Katsuyama, Tsutomu; Kanai, Masamitsu; Nakahata, Tatsutoshi; Saitoh, Hiroshi
CS Hosp., Shinshu Univ., Matsumoto, 390, Japan
SO Rinsho Byori (1992), 40(10), 1089-95
CODEN: RBYOAI; ISSN: 0047-1860
DT Journal
LA Japanese

L12 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB Nafamostat mesilate (FUT-175) **prevents** the redistribution of lysosomal enzyme and the colocalization of lysosomal hydrolases and digestive enzyme of pancreatic acinar cells in caerulein-induced acute

pancreatitis. [redacted]s, FUT-175 acts on subcellular [redacted]ganelles inside acinar cells as well as on cellular membranes and protects against pancreatitis.

AN 1991:623158 CAPLUS
DN 115:223158
TI Nafamostat mesilate **prevents** lysosomal enzyme redistribution in cerulein-induced pancreatitis
AU Hirano, Tetsuya; Manabe, Tadao; Imanishi, Katsuhiro; Ando, Katsuhiro; Kyogoku, Takahisa; Tobe, Takayoshi
CS Fac. Med., Kyoto Univ., Kyoto, Japan
SO Med. Sci. Res. (1991), 19(14), 463-4
CODEN: MSCREJ; ISSN: 0269-8951
DT Journal
LA English

L12 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB Acute pancreatitis was induced in 13 anesthetized dogs by retrograde injection of bile mixed with trypsin into the pancreatic duct. Six animals were **treated** with i.v. infusion of new synthetic antiprotease, Nafamostat Mesilate, at a dose of 1 mg/kg/h. Four out of 7 untreated animals died during the expt. All the **treated** dogs survived. Hemodynamic data were regularly monitored during a 10-h observation period. Cardiac output, mean arterial pressure and left ventricular stroke vol. decreased rapidly in the untreated animals. An increase in systemic vascular resistance and pulmonary vascular resistance was obsd. in dogs without **treatment**. Nafamostat Mesilate given as therapy significantly improved the hemodynamic parameters, and **prevented** the animals from developing shock. The study demonstrates an advantageous influence of synthetic antiprotease Nafamostat Mesilate on the course of acute exptl. pancreatitis.

AN 1991:526765 CAPLUS
DN 115:126765
TI Beneficial effect of therapeutic infusion of nafamostat mesilate (FUT-175) on hemodynamics in experimental acute pancreatitis
AU Dobosz, M.; Sledzinski, Z.; Juszkiewicz, P.; Babicki, A.; Stanek, A.; Wajda, Z.; Basinski, A.
CS 2nd Dep. Gen. Surg., Med. Acad., Gdansk, Pol.
SO Hepato-Gastroenterology (1991), 38(2), 139-42
CODEN: HEGAD4; ISSN: 0172-6390
DT Journal
LA English

L12 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The coagulation disturbance obsd. during severe acute pancreatitis before and after the infusion of a new synthetic low mol. wt. protease inhibitor (Fut-175) was compared. The coagulo-fibrinolytic changes after acute pancreatitis was induced by the intraductal injection of an autologous bile and trypsin mixt. showed decreased platelet counts, decreased plasma fibrinogen levels, prolonged partial prothrombin time and increased fibrinogen degrdn. products. In addn., markers of hypercoagulation showed increased fibrino-peptide A and decreased antithrombin III. The two markers of fibrinolysis showed increased B.beta.15-42 immunoreactive peptide and decreased .alpha.2 antiplasmin. After the infusion of Fut-175, the coagulo-fibrinolytic abnormalities, which were obsd. during severe acute pancreatitis without infusion of Fut-175, were improved. Furthermore, Fut-175 could suppress the rise in fibrino-peptide A and B.beta.15-42 immunoreactive peptide and decrease in antithrombin III and .alpha.2 antiplasmin. Thus, Fut-175 seems to be an effective inhibitor of protease-mediated hypercoagulation and fibrinolysis in severe acute pancreatitis.

AN 1991:421867 CAPLUS
DN 115:21867
TI Effect of a synthetic protease inhibitor (Fut-175) on coagulation

abnormalities during experimental acute pancreatitis in dogs
AU Satake, Katsusuke; Ha, Sin Su; Hiura, Akihito; Nishiwaki, Hideki; Haku, Aizo; Umeyama, Kaoru
CS Med. Sch., Osaka City Univ., Osaka, 545, Japan
SO Gastroenterol. Jpn. (1990), 25(6), 720-6
CODEN: GAJABC; ISSN: 0435-1339
DT Journal
LA English

L12 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The effectiveness of continuous arterial infusion of protease inhibitor on acute exptl. pancreatitis was investigated. Acute hemorrhagic pancreatitis was induced by closed duodenal loop obstruction using mongrel dogs. The obstruction was released at 16 h, and dogs were divided into three groups; Group I: non-**treated** control, Group II: nafamostat mesilate (FUT-175) was given i.v. (5 .mu.g/kg/min), Group III: FUT-175 was admitted via celiac artery. At 24 h, the concn. of FUT-175 in the pancreatic tissues in group II and III were 905 and 4453 ng/g, resp. The trypsin like activities in the pancreatic tissues in group I, II and III were 2.1, 1.4 and 0.7 nmol/min/mg protein, and the extent of necrosis of pancreatic parenchyma in each group were 49.5, 25.6 and 12.4%, resp. Serum calcium, amylase and lipase levels were significantly improved in group III. These results suggest that continuous arterial infusion of protease inhibitor markedly decreases the extent of pancreatic necrosis in severe acute pancreatitis.
AN 1990:624417 CAPLUS
DN 113:224417
TI Effect of continuous arterial infusion of protease inhibitor on experimental acute pancreatitis induced by closed duodenal loop obstruction
AU Kakugawa, Yoichiro; Takeda, Kazunori; Sunamura, Makoto; Kawaguchi, Shinya; Kobari, Masao; Matsuno, Seiki
CS Sch. Med., Tohoku Univ., Sendai, Japan
SO Nippon Shokakibyo Gakkai Zasshi (1990), 87(6), 1444-50
CODEN: NIPAA4; ISSN: 0369-4259
DT Journal
LA Japanese

L12 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB To confirm that trypsin activity is a most important indicating factor in closed duodenal loop pancreatitis in rats, the course of acute pancreatitis was obsd. when trypsinogen activation was inhibited by intraduodenal infusion of a potent synthetic trypsin inhibitor (TI, nafamostat mesilate) but the other conditions were left unchanged. Intraduodenal and intrapancreatic trypsinogen activation was inhibited for 16 h after the intraduodenal infusion of the inhibitor, although elevation of serum amylase and immunoreactive trypsin and pancreatic trypsinogen remained similar both in the TI and control groups. The mortality decreased from 44% (control) to 4% (TI) at 48 h after establishing the model. Active trypsin in duodenal reflux is an initiating factor for further development of acute pancreatitis in the closed loop model, and inhibition of the initial activation of trypsinogen has a favorable effect on acute pancreatitis even if other deleterious factors remain unchanged.
AN 1990:509072 CAPLUS
DN 113:109072
TI **Prevention** of experimental acute pancreatitis by intraduodenal trypsin inhibitor in rat
AU Ono, Hideki; Hayakawa, Tetsuo; Kondo, Takaharu; Shibata, Tokimune;

Kitagawa, Motoj[redacted]Sakai, Yuzo; Kiriyama, Seiki; [redacted]ajima, Hiroshi
CS Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SO Dig. Dis. Sci. (1990), 35(6), 787-92
CODEN: DDSCDJ; ISSN: 0163-2116
DT Journal
LA English

L12 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB OKY-046 at 30-100 mg/kg intraduodenally (i.d.) and at 1-30 mg/kg (i.v.) inhibited bronchoconstriction in a dose-dependent manner after Forssman antigen injection. Aspirin (3 mg/kg, i.v.) also suppressed bronchoconstriction. OKY-046 (30-100 mg/kg. i.d.) suppressed the increase in TXB2 in plasma in a dose-dependent manner. However, there was no effect of OKY-046 and aspirin on the decrease in complement activity (CH50), platelets, or leukocytes. Addnl., OKY-046 (300 mg. kg, p.o.) prolonged the survival time following Forssman antigen injection. However, the immune hemolysis reaction was not **prevented** by OKY-046 (10-6-10-3 M). FUT-175 protected against the Forssman shock at 1 mg/kg, i.v. and the in vitro immune hemolysis reaction at 10-5 M. OKY-046 (300 mg/kg orally) suppressed the direct passive Arthus reaction and immune complex nephritis in rats. There was no effect of OKY-046 on the delayed-type hypersensitivity response to picryl chloride in mice. OKY-046 can be a beneficial drug for the **treatment** of types II and III allergic reactions.
AN 1990:210724 CAPLUS
DN 112:210724
TI Anti-allergic effects of (E)-3-[p-(1H-imidazol-1-ylmethyl)phenyl]-2-propenoic acid (OKY-046), a specific thromboxane (TX)A2 synthetase inhibitor. (II) Effect on type II-IV allergic reactions
AU Kikuchi, Shinji; Takehana, Yasuo; Hamano, Shuichiro; Ichikawa, Kiyoshi; Komatsu, Hidetada; Okegawa, Tadao; Ikeda, Shigeru
CS Res. Lab., Kissei Pharma. Co., Ltd., Matsumoto, 399, Japan
SO Nippon Yakurigaku Zasshi (1990), 95(3), 131-7
CODEN: NYKZAU; ISSN: 0015-5691
DT Journal
LA Japanese

L12 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The inhibitory effect of Anthrobin P (I) on various enzymes in comparison with aprotinin, nafamostat mesilate and gabexate mesilate were studied in vitro. In the presence of heparin, the inhibitory effect of I on thrombin was increased .apprx.36 times and that on factor Xa was increased 38 times, while the aprotinin effect on either enzyme was not increased. The combination of I with heparin was more effective than those of nafamostat mesilate and gabexate mesilate. Its thrombin-inhibitory effect was approx. 6700 times stronger than that of gabexate mesilate and 40 times stronger than that of nafamostat mesilate. Its inhibitory effect on factor Xa was approx. 540 times stronger than that of gabexate mesilate and 4.8 times stronger than that of nafamostat mesilate. I and aprotinin did not inhibit activated protein C but both nafamostat mesilate and gabexate mesilate inhibited it with nafamostat mesilate being about 10 times more potent than gabexate mesilate. All the test substances inhibited plasmin but only gabexate mesilate and nafamostat mesilate inhibited urokinase. I did not inhibit kallikrein, while aprotinin was 69,000 times more potent than gabexate and 160 times more potent than nafamostat mesilate. Thus, I showed not only potent inhibitory effects on thrombin and factor Xa, but also a selectivity in the coagulation cascade. I did not inhibit the activity of protein C, which plays an important role in the anticoagulant system, while the other test substances did. The

results obtained here and the report about the effect of protein C on disseminated intravascular coagulation DIC suggest that I may be a favorable therapeutic drug against DIC.
AN 1990:132150 CAPLUS
DN 112:132150
TI Inhibitory effect of Anthrobin P on various proteinases
AU Abiko, Yumiko; Ohtsubo, Masayuki; Hirahara, Keizo; Matsuishi, Tetsuro
CS Pharma Res. Lab., Hoechst Japan Ltd., Japan
SO Yakuri to Chiryo (1989), 17(12), 5843-9
CODEN: YACHDS; ISSN: 0386-3603
DT Journal
LA Japanese

L12 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The effect of ONO-3307 (4-sulfamoylphenyl-4-guanidinobenzoate methanesulfonate, a new protease inhibitor, was studied on various proteases in vitro and in an exptl. thrombosis model in vivo. ONO-3307 competitively inhibited trypsin, thrombin, plasma kallikrein, plasmin, pancreatic kallikrein and chymotrypsin; the Ki values were 0.048 .mu.M, 0.18 .mu.M, 0.29 .mu.M, 0.31 .mu.M, 3.6 .mu.M and 47 .mu.M, resp. In addn., ONO-3307 inhibited both elastase release from N-formyl-Met-Leu-Phe (fMLP)-stimulated leukocytes and tissue thromboplastin release from endotoxin-stimulated leukocytes. To examine the effects of ONO-3307 on disseminated intravascular coagulation (DIC), an exptl. thrombosis model was developed. ONO-3307 (10 mg/kg/h) completely inhibited the deposition of radioactive fibrin in kidney and lung. Gabexate mesilate (50 mg/kg/h) was also effective in this model, but the effect of nafamostat mesilate was uncertain. These results indicate that ONO-3307 exhibits a wide range of inhibitory effects on various proteases, and ONO-3307 may be useful for the **treatment** of protease-mediated diseases such as thrombosis and DIC.
AN 1990:30412 CAPLUS
DN 112:30412
TI Inhibitory effects of ONO-3307 on various proteases and tissue thromboplastin in vitro and on experimental thrombosis in vivo
AU Matsuoka, Syozo; Futagami, Mayumi; Ohno, Hiroyuki; Imaki, Katsuhiro; Okegawa, Tadao; Kawasaki, Akiyoshi
CS Minase Res. Inst., Ono Pharm. Co., Ltd., Osaka, 618, Japan
SO Jpn. J. Pharmacol. (1989), 51(4), 455-63
CODEN: JJPAAZ; ISSN: 0021-5198
DT Journal
LA English

L12 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB In dogs with exptl. pancreatitis, administration of the synthetic protease inhibitor nafamostat mesilate (5 .mu.g/kg/min) markedly decreased the extent of pancreatic necrosis.
AN 1989:526779 CAPLUS
DN 111:126779
TI Effect of continuous arterial infusion of protease inhibitor on experimental acute pancreatitis
AU Kakugawa, Yoichiro; Takeda, Kazunori; Kobari, Masao; Matsuno, Seiki
CS Sch. Med., Tohoku Univ., Sendai, 980, Japan
SO Gastroenterol. Jpn. (1989), 24(4), 448
CODEN: GAJABC; ISSN: 0435-1339
DT Journal
LA English

L12 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB Recently, nontoxic synthesized low mol. wt. proteinase inhibitors have been clin. available for the **treatment** of disseminated intravascular coagulation and pancreatitis. To det. if these drugs are useful aids to **treat** patients with pemphigus, the authors examd.

the effect of .[redacted]ga.-guanidino ester analogs, i[redacted], gabexate mesylate, camostat mesylate, and nafamostat mesylate, on exptl. pemphigus acantholysis in both organ culture and neonatal BALB/c mice. Furthermore, the effect of plasma natural proteinase inhibitors (.alpha.1-proteinase inhibitor) isolated from human plasma was examd. Results revealed that low-mol. wt. inhibitors (drugs) were able to inhibit the induction of acantholysis in organ culture system, but had little or no effect on lesion formation in the neonatal mouse system. By contrast, .alpha.1-proteinase inhibitor could completely inhibit acantholysis formation in mice. These findings implied a possible new therapeutic approach using proteinase inhibitors for patients with pemphigus.

AN 1989:509005 CAPLUS
DN 111:109005
TI Proteinase inhibitors block formation of pemphigus acantholysis in experimental models of neonatal mice and skin explants: effects of synthetic and plasma proteinase inhibitors on pemphigus acantholysis
AU Naito, Katsuichi; Morioka, Shinji; Nakajima, Sumino; Ogawa, Hideoki
CS Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SO J. Invest. Dermatol. (1989), 93(1), 173-7
CODEN: JIDEAE; ISSN: 0022-202X
DT Journal
LA English

L12 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The authors examd. the ability of highly potent synthetic protease inhibitor, nafamostat mesilate (FUT-175), to protect the rat pancreas against acute pancreatitis (AP) induced by a supramaximal dose of caerulein (CR). Rats received a 6-h, continuous i.v. infusion of either CR alone or CR + a 6-h infusion of either 2.5, 5.0, 10.0, 25.0, or 50.0 mg of FUT-175/kg/h. Pancreas wts. and serum chymotrypsinogen concns. were significantly elevated by .apprx.85 and 75%, resp., over values in saline infused rats. Pancreas wts. in rats **treated** with CR + FUT-175 at doses from 2.5-25.0 mg/kg/h were significantly reduced by .apprx.20% compared to rats given CR alone, and histol. showed a redn. in the extent and size of acinar cell vacuolization and reduced interstitial edema compared to rats **treated** with CR alone. Serum chymotrypsinogen concns. in rats **treated** with CR and either 5.0 or 10.0 mg of FUT-175 kg/h were significantly lower than in rats given CR alone. Significant mortality occurred in rats infused with FUT-175 at doses of either 25.0 or 50.0 mg of FUT-175/kg/h. These data indicate that serine proteases appear to be involved in the pathogenesis of CR induced AP in rats and that FUT-175 administered in low doses (2.5-10.0 mg/kg/h) provides significant protection against this form of pancreatitis.

AN 1989:470920 CAPLUS
DN 111:70920
TI The effects of nafamostat mesilate (FUT-175) on caerulein-induced acute pancreatitis in the rat
AU Wisner, James R., Jr.; Ozawa, Susumu; Renner, Ian G.
CS Sch. Med., Univ. South. California, Los Angeles, CA, 90033, USA
SO Int. J. Pancreatol. (1989), 4(4), 383-90
CODEN: IJPNEX; ISSN: 0169-4197
DT Journal
LA English

L12 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The protease inhibitors, gabexate mesylate, nafamostat mesylate, and urinastatin (urinary trypsin inhibitor), had a protective effect against endotoxin-induced exptl. disseminated intravascular coagulation (DIC) in rats. This protective effect was noted in rats **treated** with 1, 10, or 100 mg gabexate mesylate/kg, 0.01 or 0.1 mg nafamostat mesylate/kg, and 5,000 U urinastatin/kg in the following parameters; fibrinogen and fibrin degrdn. products, fibrinogen level, prothrobmin time, partial thromboplastin time, platelet counts, and the no. of renal glomeruli with fibrin thrombi. Thus, protease inhibitors, may be useful for the

treatment of DI

AN 1989:88224 CAPLUS
DN 110:88224
TI Effect of protease inhibitors on endotoxin-induced disseminated intravascular coagulation in rats
AU Murakami, Masashi
CS 1st Dep. Med., Kyoto Prefect. Univ. Med., Kyoto, Japan
SO Kyoto-furitsu Ika Daigaku Zasshi (1988), 97(9), 1155-65
CODEN: KFIZAO; ISSN: 0023-6012
DT Journal
LA English

L12 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The **preventive** action of the new low-mol.-wt. protease inhibitor FUT-175 against acute exptl. pancreatitis (AEP) was studied in dogs. At 30 min after induction of AEP, the sensitivity of blood platelets to ADP-induced aggregation was increased >2 times in untreated animals. An evident decrease in platelet count of .apprx.37% was noted in these dogs at 6 h after AEP induction. **Treatment** of AEP with FUT-175 **prevented** these changes. Apparently, the pos. effect of FUT-175 against AEP depends at least in part on its influence on platelet aggregation.
AN 1988:522465 CAPLUS
DN 109:122465
TI Effect of FUT-175 (nafamstat mesylate) on platelets in canine acute experimental pancreatitis
AU Gabryelewicz, A.; Prokopowicz, J.; Bodzenta, A.; Bielecki, W.; Rydzewska, G.
CS Dep. Gastroenterol., Med. Acad., Bialystok, 15-276, Pol.
SO Digestion (1988), 40(1), 19-24
CODEN: DIGEBW; ISSN: 0012-2823
DT Journal
LA English

L12 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB A review, with 9 refs., of the structure, side effects, and pharmacol. of 3 new trypsin inhibitors, gabexate mesilate, camostate mesilate, and nafamostat mesilate, for the **treatment** of pancreatitis.
AN 1988:400030 CAPLUS
DN 109:30
TI New drugs for pancreatitis
AU Takeuchi, Tadashi; Shimizu, Kyoko
CS Tokyo Women's Med. Coll., Tokyo, Japan
SO Pharma Med. (1988), 6(1), 83-6
CODEN: PMEDEC; ISSN: 0289-5803
DT Journal; General Review
LA Japanese

L12 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB In rat plasma, FUT-175 exhibited a dose-dependent anticoagulant effect as detd. by its ability to prolong the activated partial thromboplastin time.
Also, I had beneficial effects in exptl. endotoxin-induced exptl. disseminated intravascular coagulation as shown by its effect in activated
partial thromboplastin time and prothrombin time, the fibrinogen and complement levels, platelet counts and fibrin degrdn. products.
AN 1988:49032 CAPLUS
DN 108:49032
TI The effects of FUT-175 (nafamostat mesilate) on blood coagulation and experimental disseminated intravascular coagulation
AU Koshiyama, Yoshiko; Kobori, Akemi; Ogihara, Madoka; Yokomoto, Yasuki; Ohtani, Kyoko; Shimamura, Kazunori; Iwaki, Masahiro
CS Res. Lab., Torii Co., Ltd., Ichikawa, 272, Japan
SO Nippon Yakurigaku Zasshi (1987), 90(6), 313-20
CODEN: NYKZAU; ISSN: 0015-5691

DT Journal
LA Japanese

L12 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB To study the role of thromboxane A2 (TxA2) [57576-52-0] in Forssman systemic shock (FSS) in guinea pigs, the effect of (E)-3-[p-(1-H-imidazol-1-ylmethyl)phenyl]-2-propenoic acid hydrochloride (OKY-046) [78712-43-3], a specific TxA2 synthetase [60832-04-4] inhibitor, was studied. OKY-046 administered i.v. clearly prolonged survival time and protected against fatal shock. In shocked animals, definite decreases in serum complement hemolytic activity (CH50), leukocyte and platelet counts, and an increase in lactate dehydrogenase activity were obsd. In addn., an increase of TXB2 and incoagulability of blood were obsd. after shock. Whereas OKY-046 had no effect on the decrease in CH50 or platelet and leukocyte counts, it inhibited the increase of TXB2 and increased the amt. of 6-keto PGF1.alpha. [58962-34-8]. When Forssman antibody (half an LD) was injected, a diphasic increase in airway resistance was obsd. OKY-046 inhibited this diphasic increase in airway resistance. These data suggest a pathophysiol. role for TxA2 in FSS. OKY-046 inhibited the Forssman antibody induced respiratory **disorders** probably due to the inhibition of TxA2 synthesis after shock.
AN 1987:168772 CAPLUS
DN 106:168772
TI Role of thromboxane (Tx) A2 in guinea pig Forssman shock and the effect of OKY-046, a Ts A2 synthetase inhibitor
AU Nagai, Hiroichi; Yakuo, Ikuhisa; Inagaki, Naoki; Koda, Akihide; Hamano, Shuichiro; Ujiie, Arao; Nakazawa, Masayuki
CS Dep. Pharmacol., Gifu Pharm. Univ., Gifu, 502, Japan
SO Prostaglandins, Leukotrienes Med. (1987), 26(2), 133-41
CODEN: PLMEDD; ISSN: 0262-1746
DT Journal
LA English

L12 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The effects of FUT-175 (I) [**82956-11-4**] on acute pancreatitis were evaluated in dogs. Models of acute pancreatitis were prepd. by the injection of 25% deoxycholic acid into pancreatic duct. The group without FUT-175 had a mortality of 64% at 24 h after pancreatitis onset, but the group with FUT-175 administration had 50%. FUT-175 had no effect on the levels of serum amylase, trypsin inhibitor capacity, and complement titer. However, FUT-175 inhibited the increase of serum trypsin [9002-07-7] levels. When trypsin (16 mg/kg) was i.v. injected, blood pressure and trypsin inhibitor capacity in the dogs were immediately decreased, and levels of serum kallikrein were increased. All dogs died within 15 min. In the group given FUT-175 before trypsin injection, improvement of blood pressure and trypsin inhibition capacity were obsd., and levels of serum kallikrein were not increased. Administration of FUT-175 may be effective in acute pancreatitis.
AN 1986:491300 CAPLUS
DN 105:91300
TI Effects of FUT-175 on experimental acute pancreatitis and on trypsin-injected dogs
AU Tanaka, Tatsuhiko; Yamamoto, Masahiro; Okumura, Shuuichi; Kasiwagi, Ryouichi; Oyanagi, Harumasa; Saitoh, Yoichi
CS Sch. Med., Kobe Univ., Kobe, Japan
SO Yakuri to Chiryo (1986), 14(4), 2241-7
CODEN: YACHDS; ISSN: 0386-3603

DT Journal
LA Japanese

L12 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB In dogs during 300-min recovery from a circulatory arrest, the improvement of disseminated intravascular coagulation (DIC) in gabexate mesilate (FOY) [56974-61-9]-and Nafamstat mesilate (FUT 175) [**82956-11-4**]-**treated** groups was better than that in a heparin [9005-49-6]-**treated** group. A decrease in platelet counts and antithrombin III (AT-III) concns in the blood seen in the controls was cor. by heparin but the increased concns. of fibrin degrdn. product (FDP) were unchanged in the heparin-**treated** group. Prothrombin time, activated partial prothrombin time (APTT) and FDP levels remained within normal limits in the FOY-**treated** group and no decrease in either platelet count or AT-III concns. was obsd. In the FUT 175-**treated** group, prolongation of APTT, no decrease in the platelet count and AT-III concns., and normal FDP levels were obsd. The results indicated the importance of early **treatment** for DIC.
AN 1986:61730 CAPLUS
DN 104:61730
TI Studies on the effects of primary therapy for DIC following circulatory arrest
AU Tanaka, Shigeru; Takemoto, Yoshinobu; Nakamura, Yoshihiro; Kohama, Akitsugu
CS Dep. Emerg. Med., Kawasaki Med. Sch., Japan
SO Kawasaki Igakkaishi (1984), 10(4), 501-5
CODEN: KAIGD3; ISSN: 0386-5924
DT Journal
LA Japanese

L12 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The effects of FUT-175 (nafamstat mesylate) (I) [**82956-11-4**], a potent proteinase [9001-92-7] inhibitor, on acute pancreatitis (serum levels of pancreatic enzymes and histol. changes of various organs) were compared in 2 groups of dogs with exptl. acute pancreatitis induced by sodium deoxycholate. During const. i.v. infusion of 10 .mu.g/kg/h of I for 3 h, the serum concn. of the drug remained high, whereas the elevated trypsin-like activity in serum of the pancreatitis dogs was decrease, suggesting proteinase inhibition. Levels of the other pancreatic enzymes in serum of the pancreatitis dogs decreased slightly in the I-**treated** group. Furthermore, histol. changes of the pancreas were less in I-**treated** dogs, whereas the other organs including lung and kidney did not show any difference in their histol. pictures. Pancreatic enzymes were seen in ascites, 12.apprx.24 h after induction of exptl. acute pancreatitis, and levels were markedly higher than the serum levels in the same individuals; these levels were not suppressed by the i.v. infusion of I. Apparently, the progress of acute inflammatory changes of the pancreas can be protected by I administration, and it may be possible that the **treatment** of multiple organ failure (thought to be caused by various enzymes) and the **treatment** for ascites accumulation or ascitic enzymes is necessary in moderate or severe acute pancreatitis.
AN 1985:572036 CAPLUS
DN 103:172036
TI Efficacy of a proteinase inhibitor on experimental acute pancreatitis in dogs
AU Taguchi, Susumu; Usui, Mitsuro; Nagumo, Akihiko; Funatomi, Hitoshi; Hatta, Yoshio
CS Sch. Med., Showa Univ., Tokyo, Japan
SO Yakuri to Chiryo (1985), 13(6), 3367-76
CODEN: YACHDS; ISSN: 0386-3603
DT Journal

LA Japanese

L12 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB FUT-175 (I) [**82956-11-4**], a new synthetic protease [9001-92-7] inhibitor, was administered to (NZB .times. NZB)F1 mice in order to examine its influence on the development of autoimmune diseases. I has both prophylactic and curative effects on the development of lupus nephritis: the I **treated** mice showed a low percentage of proteinuria, a marked decrease in blood urea N levels, and low glomerular damages. Dexamethasone [50-02-2] had almost the same effect as I, but it was slightly less effective than I. These results suggest that the administration of I may become a viable strategy for the **treatment** of human autoimmune diseases.
AN 1985:571628 CAPLUS
DN 103:171628
TI Effect of FUT-175, a new synthetic protease inhibitor, on the development of lupus nephritis in (NZB .times. NZW) F1 mice
AU Ikehara, S.; Shimamura, K.; Aoyama, T.; Fujii, S.; Hamashima, Y.
CS Fac. Med., Kyoto Univ., Kyoto, 606, Japan
SO Immunology (1985), 55(4), 595-600
CODEN: IMMUAM; ISSN: 0019-2805
DT Journal
LA English

L12 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB In the acute serum sickness model in rabbits, platelet release of 5-HT [50-67-9], platelet surface Igs, and platelet aggregation in response to ADP [58-64-0], together with the effect of dipyridamole [58-32-2] and the complement C1r [80295-34-7] antagonist FUT-175 [**82956-11-4**] was examd. The immune release of 5-HT from platelets occurred between 4 and 6 days after injection of bovine serum albumin (BSA), before immune elimination and proteinuria, but coincident with the appearance of immune complexed BSA in the circulation. Nevertheless, platelet turnovers were not accelerated. **Treatment** with dipyridamole 50 mg/kg/24 h **prevented** the release of 5-HT and inhibited proteinuria, glomerular hypercellularity and immune complexes in the glomeruli. Using the C1r antagonist FUT-175, similar abrogation of the disease was obtained. Thus, in the nephritis of acute serum sickness in rabbits, some of the immune release from platelets may be the result of immune complex binding to the platelet, perhaps through the receptor for complement C3b [80295-43-8].
AN 1985:553616 CAPLUS
DN 103:153616
TI Platelet involvement in the nephritis of acute serum sickness in rabbits: protection by dipyridamole and FUT-175
AU Koyama, A.; Inage, H.; Sano, M.; Narita, M.; Tojo, S.; Neild, G. H.; Cameron, J. S.
CS Inst. Clin. Med., Univ. Tsukuba, 30305, Japan
SO Clin. Exp. Immunol. (1985), 61(2), 388-96
CODEN: CEXIAL; ISSN: 0009-9104
DT Journal
LA English

L12 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB Ascitic fluid from dogs with hemorrhagic pancreatitis induced by intraductal injection of trypsin and autologous bile contained high concns. of trypsin, esterase, bradykinin, histamine, and prostaglandin E. When this ascitic fluid was injected i.p. into mice in doses of 2 and 3 mL, the mortality rate 72 h after injection was 66.0 and 88.4%, resp. When nafamstat mesilate (a synthetic antiprotease) was mixed with the ascitic fluid before injection, trypsin was not detected, and bradykinin and esterase were decreased considerably. The mortality rate for this mixt. at 2 and 3 mL injections was 26.7 and 80.6%, resp. Bradykinin,

trypsin, and es[redacted]ase of ascitic fluid may be pa[redacted]y responsible for the high mortality rate obsd. in pancreatitis. Peritoneal lavage solns. with nafamstat mesilate may be effective in hemorrhagic pancreatitis therapy.

AN 1985:502878 CAPLUS
DN 103:102878
TI Toxic products in hemorrhagic ascitic fluid generated during experimental acute hemorrhagic pancreatitis in dogs and a **treatment** which reduces their effect
AU Satake, Katsusuke; Koh, Ichikun; Nishiwaki, Hidiki; Umeyama, Kaoru
CS Med. Sch., Osaka City Univ., Osaka, 545, Japan
SO Digestion (1985), 32(2), 99-105
CODEN: DIGEBW; ISSN: 0012-2823
DT Journal
LA English

L12 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2000 ACS
AB The effect of FUT-175 (I) [**82956-11-4**] on various models of exptl. acute pancreatitis were examd. FUT-175 infused i.v. in a dose range of 5-50 .mu.g/kg/min inhibited the increase in plasma trypsin activity and reduced the mortality of rabbits in trypsin-induced acute pancreatitis in a dose-dependent manner. Increases in serum amylase activity and pancreatic tissue lesions were attenuated by FUT-175. FUT-175 infused i.v. in a dose range of 1-50 .mu.g/kg/min decreased the mortality of rats in exptl. acute pancreatitis produced by trypsin and endotoxin. FUT-175 infused i.v. at a dose range 1-100 .mu.g/kg/min protected the dogs from the increase in plasma trypsin activity and hypotension and shock induced by trypsin.

AN 1984:622249 CAPLUS
DN 101:222249
TI Pharmacological studies of FUT-175, nafamstat mesylate. II. Effects on experimental acute pancreatitis
AU Iwaki, Masahiro; Ozeki, Masayuki; Sato, Takuo; Suzuki, Kunihiko; Motoyoshi, Akemi; Suzuki, Shoshi; Fujita, Mitsunobu; Aoyama, Takuo
CS Res. Lab., Torii and Co., Ltd., Ichikawa, 272, Japan
SO Nippon Yakurigaku Zasshi (1984), 84(4), 363-72
CODEN: NYKZAU; ISSN: 0015-5691
DT Journal
LA Japanese

=> s ?mycardial? or ?infarction?

L13 228126 ?MYCARDIAL? OR ?INFARCTION?

=> s l1 and l13

L14 4 L1 AND L13

=> d 1-4 ab,bib

L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2000 ACS
AB Diagnostic methods that rely on the use of one or more assays that assess cellular activation are provided. The assays are performed on whole blood or leukocytes (neutrophils), and indicate individually or in combination the level of cardiovascular cell activation, which is pivotal in many chronic and acute disease states. These results of the assays are used within a clin. framework to support therapeutic decisions such as: further testing for infectious agents, anti-oxidant or anti-adhesion therapy, postponement and optimal re-scheduling of high-risk surgeries, classifying susceptibility to and progression rates of chronic disease such as diabetes, organ rejection, atherogenesis, and venous insufficiency; extreme interventions in trauma cases of particularly high risk and

activation-lowering therapies. Also provided is a cell lysate derived from a pancreatic homogenate that contains circulating cell activating factors, which can serve as targets for drug screening to identify drug candidates for use in activation lowering therapies. Methods for lowering cell activation by administering protease inhibitors, particularly serine protease inhibitors, are also provided. Kits for performing the methods are also provided.

AN 1999:595348 CAPLUS
DN 131:225828
TI Methods of diagnosis and triage using cell activation measures
IN Stoughton, Roland B.; Schmid-Schonbein, Geert W.; Hugli, Tony E.; Kistler, Erik
PA Cell Activation, Inc., USA; The Regents of the University of California; The Scripps Research Institute
SO PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9946367	A2	19990916	WO 1999-US5247	19990311
WO 9946367	A3	19991209		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9931829	A1	19990927	AU 1999-31829	19990311
PRAI US 1998-38894		19980311		
WO 1999-US5247		19990311		

L14 ANSWER 2 OF 4 USPATFULL
AB The present invention is directed to thrombo-resistant coatings for use with gas permeable biomedical devices and implants. The coatings include a siloxane surface onto which a plurality of amine functional groups have been bonded. Covalently bonded to the amine functional groups are a plurality of poly(ethylene oxide) chains, such that a single poly(ethylene oxide) chain is bonded to a single amine functional group. A quantity of at least one bioactive molecule designed to counteract a specific blood-material incompatibility reaction is covalently bonded to the poly(ethylene oxide) chains, such that a single bioactive molecule is coupled to a single polyethylene oxide chain.

The methods of manufacturing the present invention include preparing a material having a siloxane surface onto which a plurality of amine functional groups have been bonded. This is preferably achieved by plasma etching with ammonia gas. The amine-containing siloxane surface is reacted with poly(ethylene oxide) chains terminated with functional groups capable of reacting with the amine groups on the siloxane surface. The material is then reacted with a solution of at least one bioactive molecule which counteracts a blood-material incompatibility reaction, such that a single bioactive molecule is coupled to a single poly(ethylene oxide) chain. The resulting siloxane surface is capable of resisting blood-material incompatibility reactions while maintaining high gas permeability.

AN 94:71052 USP[redacted]ULL
TI Gas permeable thrombo-resistant coatings and methods of manufacture
IN Winters, Suzanne, Salt Lake City, UT, United States
Solen, Kenneth A., Orem, UT, United States
Sanders, Clifton G., Salt Lake City, UT, United States
Mortensen, JD, Sandy, UT, United States
Berry, Gaylord, Salt Lake City, UT, United States
PA Cardiopulmonics, Inc., Salt Lake City, UT, United States (U.S. corporation)
PI US 5338770 19940816
AI US 1990-509063 19900412 (7)
DCD 20101116
RLI Continuation-in-part of Ser. No. US 1988-215014, filed on 5 Jul 1988, now patented, Pat. No. US 5262451 which is a continuation-in-part of Ser. No. US 1988-204115, filed on 8 Jun 1988, now patented, Pat. No. US 4850958
DT Utility
EXNAM Primary Examiner: Szekely, Peter
LREP Workman Nydegger Jensen
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1122
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS
AB Background: Reperfusion injury in the myocardium has recently been considered to be a type of inflammation, and close attention has been paid to the possible involvement of neutrophils, complement, and cytokines in the onset of this injury. Recently, it has been reported that serum levels of interleukin-6 are elevated significantly after myocardial **infarction**. The major site of interleukin-6 production and its exact roles are still unknown. In this study, we hypothesized that myocytes may produce interleukin-6 during hypoxia and this may play a role in neutrophil-mediated reperfusion injury. Methods and results: In the clinical study, 20 patients who underwent coronary artery bypass grafting were divided into 2 groups: group F, in which patients were treated with a serine protease inhibitor (FUT-175, 2 mg/kg per hour) during cardiopulmonary bypass, and group C (untreated patients). In group C, myocardial interleukin-6 production, as determined by the difference between the interleukin-6 level in the cardiopulmonary bypass circuit and its level in coronary venous blood, increased significantly after reperfusion (12 +- 4 pg/mL) as compared with that before aortic crossclamping (2 +- 2 pg/mL). In group F, the increase in the interleukin-6 level was suppressed significantly (before aortic crossclamping, 3 +- 2 pg/mL; after reperfusion, 4 +- 3 pg/mL). The interleukin-6 production differed significantly between group C and group F. In the in vitro experimental study, the supernatant from myocytes exposed to 2 hours of hypoxia (group 2H) showed significantly higher levels of interleukin-6 (455 +- 260 pg/mL) than that from normoxic myocytes (group N) (47 +- 15 pg/mL). This interleukin-6 production was suppressed by the addition of FUT-175 (123 +- 24 pg/mL). The interleukin-6 production by endothelial cells of coronary vessels did not differ between group 2H (283 +- 151 pg/mL) and group N (151 +- 86 pg/mL). In a coincubation system with a monolayer of endothelial cells on collagen membrane and myocytes under collagen membrane in a modified Boyden chamber, 2 hours of coincubation showed a significantly higher percent of neutrophil transendothelial migration (group 2H vs N, 78% +- 13% vs 26% +- 11%), value of chemiluminescence (22 +- 8 vs 5 +- 2 X 103 counts/3

minutes), and p[redacted]ent of irreversibly damaged my[redacted]tes (48% +- 17% vs 12% +- 8%) than norm[redacted]ic coincubation. In contrast, a[redacted]i-interleukin-6 monoclonal antibody significantly attenuated neutrophil transendothelial migration (42% +- 19%) and irreversible damage of myocytes (26% +- 15%) in
2 hours of coincubation. Conclusions: Interleukin-6 is produced from myocardium during ischemia and reperfusion in patients undergoing coronary
bypass grafting. This interleukin-6 may be derived from hypoxic myocytes and play a role in neutrophil-mediated reperfusion injury in myocardium.

AN 1998:475040 BIOSIS
DN PREV199800475040
TI Interleukin-6 derived from hypoxic myocytes promotes neutrophil-mediated reperfusion injury in myocardium.
AU Sawa, Yoshiki (1); Ichikawa, Hajime; Kagisaki, Koji; Ohata, Toshihiro; Matsuda, Hikaru
CS (1) First Dep. Surg., Osaka Univ. Med. Sch., 2-2 Yamada-oka, Suita, Osaka 565 Japan
SO Journal of Thoracic and Cardiovascular Surgery, (Sept., 1998) Vol. 116, No. 3, pp. 511-517.
ISSN: 0022-5223.
DT Article
LA English

L14 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS
AB The therapeutic effect of the synthetic serine protease inhibitor, FUT-175, on cerebral vasospasm after subarachnoid hemorrhage (SAH) was investigated. Twenty-three patients with severe SAH who were admitted btween February and July 1990 and who underwent surgery within 48 hours of
the initial aneurysmal rupture were treated with an intravenous administration of FUT-175 soon after the operation. The patietns were divided randomly into three groups, each receiving a different dose of FUT-175 (Group A, 20 mg every 12 hours for 4 days; Group B, 20 mg every 6 hours for 4 days, Group C, 40 mg every 6 hours for 4 days). The results were compared with another group of twenty-two patients with severe SAH who were admitted before February 1990 and received equivalent treatment, except they were not treated with FUT-175. In 64% of all the patients treated with FUT-175 (Groups A, B, C), and in 85% of those treated with higher doses of FUT-175 (Groups B and C), there was no spasm or only mild vasospasm on the angiogram. The incidence of a delayed ischemic neurological deficit significantly decreased from 55% in the control group
to 13% in all patients treated with FUT-175 and to 7% in the patients treated with higher doses ($P < 0.05$). The incidence of cerebral **infarction** resulting from vasospasm significantly decreased from 43% in the control group to 9% in patients treated with FUT-175. In the patients treated with higher doses of FUT-175 (Groups B and C), none developed cerebral **infarction**. The outcome 1 month after SAH also significantly improved in patients treated with FUT-175. The patients
with a good outcome accounted for 67% of the patients treated with FUT-175, as compared with 35% in the control group. The patients with a poor outcome accounted for only 9% of patients treated with FUT-175, as compared with 36F% in the control group. These figures were much more satisfactory in the patients treated with higher doses of FUT-175, i.e., 71% of the patients had a good outcome and none had a poor outcome. FUT-175 is a promising drug for preventing cerebral vasospasm and delayed ischemic neurological defict after SAH. Additional controlled studies with
larger numbers of patients are necessary.

AN 1992:215286 BIOSIS
DN BA93:115511
TI THERAPEUTIC TRIAL OF CEREBRAL VASOSPASM WITH THE SERINE PROTEASE INHIBITOR
FUT-175 ADMINISTERED IN THE ACUTE STAGE AFTER SUBARACHNOID HEMORRHAGE.

AU YANAMOTO H; KIK[redacted] H; SATO M; SHIMIZU Y; YONEDA[redacted] OKAMOTO S
CS DEP. NEUROSURGERY, KYOTO UNIV. MED. SCH., KAWAHARA-CHO 54, SYOGOIN, SAKYO-KU, KYOTO, JPN.
SO NEUROSURGERY (BALTIMORE), (1992) 30 (3), 358-363.
CODEN: NRSRDY.
FS BA; OLD
LA English